

Figure 1

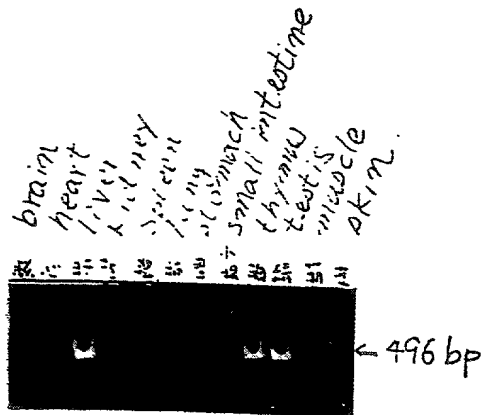
| | | |
|--------------|---|-----|
| human FGF-21 | MDSDETGFHSGLWWSVLGALLGACQAHIPDSSPLLQFG-GQV-RQRYLYTD | 52 |
| mouse FGF- | MARKWNGRAVARALVLATLWLAVS-GRPLAQ-QSQSVSDEDPFLFYGWGKITRLQYLYSA | 58 |
| | DAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGLY | 112 |
| | GPYVSNCFIRSDGSDCEEDQNERNLIEFRAVALKTIKIDVSSVRYLCMSADGKIYG | 118 |
| | SLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPP | 172 |
| | LIRYSEEDCTFREEMDCLGYNQYRSMKHHLHIIIFIQAK-PREQLQDQKPSNFIPVFHRSF | 177 |
| | ALPEPPGILAPQ--PPDVGSSDPLSMVGPSQG--RSPSYAS | |
| | FETGDQLRSKMFSLPLESDSMDPFRMVEDVDHLVKSPSFQK | |

| | |
|--------------|---|
| human FGF-21 | MDSDETFGEHSLWVSLAGLLG-ACQAHPIPDSSPLLQF--GGQVRQRYLYTDDAQQ- * **** * * * * 56 |
| human FGF-19 | MMSGCVVHVW--ILAGLWLAAGRPLAFSDAGPHVHYGWGDP IRLRHL YTSGPHGL 55 |
| | TEAHLEIREDTGVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGS LHF * * * * * 116 |
| | SSCFLIRADGVVDCARGQSAHSLLLEIKAVALTVAIKGVHVSRYLCMGADGKMQGLLQY 115 |
| | DPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPH--RDPAPRGPARFLPLPGLPPAL * * * * * 174 |
| | SEEDCAFEIEIRPDGYNVYRSEKHRLPVSLSAKQRQLYKNRGFLPLSHFLPMLPMVPEE 175 |
| | PEP-PGILAPQ----PPDVGSSDPLSMV-GPSQGRSPSYAS 209 * * * * * 216 |
| | PEDLRGHLESDMFSSPLETDSMDPFGLVTGLEAVRSPSFEK 216 |

Figure 2

Figure 3

PCR



Northern

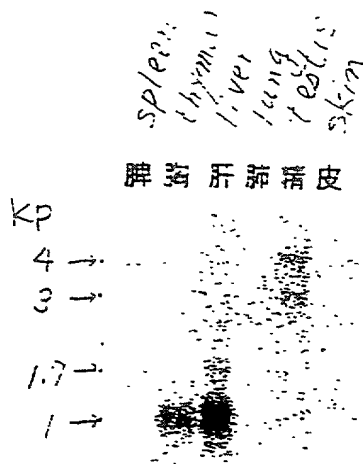


Figure 4

Filename : mouse FGF-21 cDNA in pGEM-T
Sequence Size : 659
Sequence Position: 1 - 659
Translation Position: 14 - 646;

10 20 30 40 50 60
GAGCGCAGCCCTGATGGAATGGATGAGATCTAGAGTTGGGACCCCTGGGACTGTGGGTCCG SEQ ID NO:1
M E W M R S R V G T L G L W V R SEQ ID NO:2

70 80 90 100 110 120
ACTGCTGCTGGCTGTCTTCCTGCTGGGGGTCTACCAAGCATACCCATCCCTGACTCCAG
L L L A V F L L G V Y Q A Y P I P D S S -

130 140 150 160 170 180
CCCCCTCCTCAGTTTGGGGGTCAAGTCCGGCAGAGGTACCTCTACACAGATGACGACCA
P L L Q F G G Q V R Q R Y L Y T D D D Q

190 200 210 220 230 240
AGACACTGAAGCCACCTGGAGATCAGGGAGGATGGAACAGTGGTAGGCGCAGCACACCG
D T E A H L E I R E D G T V V G A A H R

250 260 270 280 290 300
CAGTCCAGAAAGTCTCCTGGAGCTCAAAGCCTTGAAGCCAGGGGTCAATCAAATCCTGGG
S P E S L L E L K A L K P G V I Q I L G

310 320 330 340 350 360
TGTCAAAGCCTCTAGGTTTCTTTGCCAACAGCCAGATGGAGCTCTCTATGGATCGCCTCA
V K A S R F L C Q Q P D G A L Y G S P H

370 380 390 400 410 420
CTTTGATCCTGAGGCCTGCAGCTTCAGAGAACTGCTGCTGGAGGACGGTTACAATGTGTA
F D P E A C S F R E L L L E D G Y N V Y

430 440 450 460 470 480
CCAGTCTGAAGCCCATGGCCTGCCCCTGCGTCTGCCTCAGAAGGACTCCCCAAACAGGA
Q S E A H G L P L R L P Q K D S P N Q D

490 500 510 520 530 540
TGCAACATCCTGGGGACCTGTGCGCTTCTGCCCATGCCAGGCCTGCTCCACGAGCCCCA
A T S W G P V R F L P M P G L L H E P Q

550 560 570 580 590 600
AGACCAAGCAGGATTCTGCCCCCAGAGCCCCCAGATGTGGGCTCCTCTGACCCCTGAG
D Q A G F L P P E P P D V G S S D P L S

610 620 630 640 650 660
CATGGTAGAGCCTTTACAGGGCCGAAGCCCCAGCTATGCGTCTGACTTTCTCTGAATC
M V E P L Q G R S P S Y A S *

Figure 5

Filename : human FGF-21 cDNA in pGEM-T
Sequence Size : 643
Sequence Position: 1 - 643
Translation Position: 9 - 638;

```

      10      20      30      40      50      60
agccattgatggactcggacgagaccgggttcgagcactcaggactgtgggtttctgtgc
      M D S D E T G F E H S G L W V S V L
                                         SEQ ID NO:3
                                         SEQ ID NO:4

      70      80      90     100     110     120
tggttggtcttctgtctgggagcctgccaggcacaccccatccctgactccagtcctctcc
      A G L L L G A C Q A H P I P D S S P L L

      130     140     150     160     170     180
tgcaattcgggggccaagtccggcagcgggtacctctacacagatgatgccagcagacag
      Q F G G Q V R Q R Y L Y T D D A Q Q T E

      190     200     210     220     230     240
aagccacctggagatcagggaggatgggacggtggggggcgctgctgaccagagccccc
      A H L E I R E D G T V G G A A D Q S P E

      250     260     270     280     290     300
aaagtctcctgcagctgaagccttgaagccgggagttattcaaatcttgggagtaaga
      S L L Q L K A L K P G V I Q I L G V K T

      310     320     330     340     350     360
catccaggttcctgtgccagcggccagatggggccctgtatggatcgctccactttgacc
      S R F L C Q R P D G A L Y G S L H F D P

      370     380     390     400     410     420
ctgaggcctgcagcttcgggagctgttcttgaggacggatacaatgtttaccagtccg
      E A C S F R E L L L E D G Y N V Y Q S E

      430     440     450     460     470     480
aagccacggcctcccgctgcacctgccagggaacaagtccccacacggggacctgcac
      A H G L P L H L P G N K S P H R D P A P

      490     500     510     520     530     540
cccgaggaccagctcgcttctgccaactaccaggcctgcccccgcaactcccgagccac
      R G P A R F L P L P G L P P A L P E P P

      550     560     570     580     590     600
ccggaatcctggccccccagcccccgatgtgggtcctcctcgaccctctgagcatgggtg
      G I L A P Q P P D V G S S D P L S M V G

      610     620     630     640     650
gaccttccagggccgaagccccagctacgcttctgaagcca
      P S Q G R S P S Y A S *

```

Figure 6

| | | |
|--------------|---|-----|
| human FGF-21 | MDSDETGFEHSLWVS-VLAGLLLGACQAHPDSSPLLQFGGQVRQRYLYTDDAQQTEA | 59 |
| | * **** ** ** **** | |
| mouse FGF-21 | MEWMRSRVGTLGLWVRLLLAVFLLGVYQAYPIPDSSPLLQFGGQVRQRYLYTDDDDQTEA | 60 |
| | | |
| | HLEIREDTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGGALYGSILHFDPE | 119 |
| | ***** ** **** | |
| | HLEIREDTVGGAHRSPELLELKALKPGVIQILGVKASRFLCQRPDGGALYGSPLHFDPE | 120 |
| | | |
| | ACSFRELLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPALPEPPG | 179 |
| | ***** ** **** | |
| | ACSFRELLEDGYNVYQSEAHGLPLRLPQKDSPNQDATSWGVPVRFLLPMPGLLHEPQDQAG | 180 |
| | | |
| | ILAPQPPDVGSSDPLSMWGPSQGRSPSYAS | 209 |
| | * * **** | |
| | FLPPEPPDVGSSDPLSMWEPLQGRSPSYAS | 210 |

Figure 7A

Codon usage for yeast (highly expressed) genes

| AmAcid | Codon | Number | /1000 | Fraction | .. |
|--------|-------|---------|-------|----------|----|
| Gly | GGG | 33.00 | 0.86 | 0.01 | |
| Gly | GGA | 70.00 | 1.82 | 0.02 | |
| Gly | GGT | 2672.00 | 69.62 | 0.91 | |
| Gly | GGC | 171.00 | 4.46 | 0.06 | |
| Glu | GAG | 277.00 | 7.22 | 0.10 | |
| Glu | GAA | 2442.00 | 63.63 | 0.90 | |
| Asp | GAT | 1100.00 | 28.66 | 0.48 | |
| Asp | GAC | 1211.00 | 31.55 | 0.52 | |
| Val | GTG | 117.00 | 3.05 | 0.04 | |
| Val | GTA | 75.00 | 1.95 | 0.03 | |
| Val | GTT | 1548.00 | 40.33 | 0.56 | |
| Val | GTC | 1026.00 | 26.73 | 0.37 | |
| Ala | GCG | 36.00 | 0.94 | 0.01 | |
| Ala | GCA | 203.00 | 5.29 | 0.06 | |
| Ala | GCT | 2221.00 | 57.87 | 0.65 | |
| Ala | GCC | 969.00 | 25.25 | 0.28 | |
| Arg | AGG | 20.00 | 0.52 | 0.01 | |
| Arg | AGA | 1336.00 | 34.81 | 0.83 | |
| Ser | AGT | 116.00 | 3.02 | 0.05 | |
| Ser | AGC | 94.00 | 2.45 | 0.04 | |
| Lys | AAG | 2365.00 | 61.62 | 0.78 | |
| Lys | AAA | 651.00 | 16.96 | 0.22 | |
| Asn | AAT | 347.00 | 9.04 | 0.22 | |
| Asn | AAC | 1259.00 | 32.80 | 0.78 | |
| Met | ATG | 766.00 | 19.96 | 1.00 | |
| Ile | ATA | 43.00 | 1.12 | 0.02 | |
| Ile | ATT | 1223.00 | 31.87 | 0.52 | |
| Ile | ATC | 1070.00 | 27.88 | 0.46 | |
| Thr | ACG | 28.00 | 0.73 | 0.01 | |

Table 0.0000

Figure 7 B

| | | | | |
|-----|-----|---------|-------|------|
| Thr | ACA | 126.00 | 3.28 | 0.06 |
| Thr | ACT | 1129.00 | 29.42 | 0.50 |
| Thr | ACC | 962.00 | 25.07 | 0.43 |
| Trp | TGG | 325.00 | 8.47 | 1.00 |
| End | TGA | 10.00 | 0.26 | 0.09 |
| Cys | TGT | 254.00 | 6.62 | 0.89 |
| Cys | TGC | 33.00 | 0.86 | 0.11 |
| End | TAG | 11.00 | 0.29 | 0.10 |
| End | TAA | 85.00 | 2.21 | 0.80 |
| Tyr | TAT | 219.00 | 5.71 | 0.19 |
| Tyr | TAC | 913.00 | 23.79 | 0.81 |
| Leu | TTG | 2202.00 | 57.38 | 0.69 |
| Leu | TTA | 576.00 | 15.01 | 0.18 |
| Phe | TTT | 432.00 | 11.26 | 0.27 |
| Phe | TTC | 1145.00 | 29.83 | 0.73 |
| Ser | TCG | 26.00 | 0.68 | 0.01 |
| Ser | TCA | 149.00 | 3.88 | 0.06 |
| Ser | TCT | 1279.00 | 33.33 | 0.52 |
| Ser | TCC | 818.00 | 21.31 | 0.33 |
| Arg | CGG | 0.00 | 0.00 | 0.00 |
| Arg | CGA | 1.00 | 0.03 | 0.00 |
| Arg | CGT | 249.00 | 6.49 | 0.15 |
| Arg | CGC | 5.00 | 0.13 | 0.00 |
| Gln | CAG | 62.00 | 1.62 | 0.05 |
| Gln | CAA | 1225.00 | 31.92 | 0.95 |
| His | CAT | 236.00 | 6.15 | 0.35 |
| His | CAC | 433.00 | 11.28 | 0.65 |
| Leu | CTG | 52.00 | 1.35 | 0.02 |
| Leu | CTA | 236.00 | 6.15 | 0.07 |
| Leu | CTT | 90.00 | 2.35 | 0.03 |
| Leu | CTC | 14.00 | 0.36 | 0.00 |
| Pro | CCG | 10.00 | 0.26 | 0.01 |
| Pro | CCA | 1271.00 | 33.12 | 0.80 |
| Pro | CCT | 279.00 | 7.27 | 0.18 |
| Pro | CCC | 33.00 | 0.86 | 0.02 |

408D1 130.2011 / PP-16758.003

Figure 8 A

Codon usage for Drosophila (highly expressed) genes

| AmAcid | Codon | Number | /1000 | Fraction | .. |
|--------|-------|---------|-------|----------|----|
| Gly | GGG | 6.00 | 0.28 | 0.00 | |
| Gly | GGA | 380.00 | 18.04 | 0.22 | |
| Gly | GGT | 575.00 | 27.29 | 0.34 | |
| Gly | GGC | 746.00 | 35.41 | 0.44 | |
| Glu | GAG | 1217.00 | 57.77 | 0.91 | |
| Glu | GAA | 115.00 | 5.46 | 0.09 | |
| Asp | GAT | 503.00 | 23.88 | 0.43 | |
| Asp | GAC | 654.00 | 31.04 | 0.57 | |
| Val | GTG | 719.00 | 34.13 | 0.45 | |
| Val | GTA | 29.00 | 1.38 | 0.02 | |
| Val | GTT | 226.00 | 10.73 | 0.14 | |
| Val | GTC | 608.00 | 28.86 | 0.38 | |
| Ala | GCG | 94.00 | 4.46 | 0.05 | |
| Ala | GCA | 80.00 | 3.80 | 0.04 | |
| Ala | GCT | 446.00 | 21.17 | 0.24 | |
| Ala | GCC | 1277.00 | 60.61 | 0.67 | |
| Arg | AGG | 48.00 | 2.28 | 0.06 | |
| Arg | AGA | 12.00 | 0.57 | 0.01 | |
| Ser | AGT | 16.00 | 0.76 | 0.01 | |
| Ser | AGC | 267.00 | 12.67 | 0.23 | |
| Lys | AAG | 1360.00 | 64.55 | 0.93 | |
| Lys | AAA | 108.00 | 5.13 | 0.07 | |
| Asn | AAT | 127.00 | 6.03 | 0.13 | |
| Asn | AAC | 878.00 | 41.67 | 0.87 | |
| Met | ATG | 387.00 | 18.37 | 1.00 | |
| Ile | ATA | 4.00 | 0.19 | 0.00 | |
| Ile | ATT | 390.00 | 18.51 | 0.29 | |
| Ile | ATC | 969.00 | 45.99 | 0.71 | |

Figure 8 B

| | | | | |
|-----|-----|---------|-------|------|
| Thr | ACG | 114.00 | 5.41 | 0.08 |
| Thr | ACA | 34.00 | 1.61 | 0.02 |
| Thr | ACT | 164.00 | 7.78 | 0.11 |
| Thr | ACC | 1127.00 | 53.49 | 0.78 |
| Trp | TGG | 243.00 | 11.53 | 1.00 |
| End | TGA | 1.00 | 0.05 | 0.01 |
| Cys | TGT | 20.00 | 0.95 | 0.08 |
| Cys | TGC | 220.00 | 10.44 | 0.92 |
| End | TAG | 12.00 | 0.57 | 0.17 |
| End | TAA | 58.00 | 2.75 | 0.82 |
| Tyr | TAT | 113.00 | 5.36 | 0.16 |
| Tyr | TAC | 574.00 | 27.25 | 0.84 |
| Leu | TTG | 210.00 | 9.97 | 0.12 |
| Leu | TTA | 9.00 | 0.43 | 0.01 |
| Phe | TTT | 62.00 | 2.94 | 0.09 |
| Phe | TTC | 635.00 | 30.14 | 0.91 |
| Ser | TCG | 195.00 | 9.26 | 0.17 |
| Ser | TCA | 29.00 | 1.38 | 0.02 |
| Ser | TCT | 103.00 | 4.89 | 0.09 |
| Ser | TCC | 558.00 | 26.49 | 0.48 |
| Arg | CGG | 7.00 | 0.33 | 0.01 |
| Arg | CGA | 25.00 | 1.19 | 0.03 |
| Arg | CGT | 281.00 | 13.34 | 0.34 |
| Arg | CGC | 465.00 | 22.07 | 0.55 |
| Gln | CAG | 703.00 | 33.37 | 0.91 |
| Gln | CAA | 66.00 | 3.13 | 0.09 |
| His | CAT | 88.00 | 4.18 | 0.22 |
| His | CAC | 312.00 | 14.81 | 0.78 |
| Leu | CTG | 1182.00 | 56.10 | 0.69 |
| Leu | CTA | 21.00 | 1.00 | 0.01 |
| Leu | CTT | 55.00 | 2.61 | 0.03 |
| Leu | CTC | 224.00 | 10.63 | 0.13 |
| Pro | CCG | 84.00 | 3.99 | 0.09 |
| Pro | CCA | 135.00 | 6.41 | 0.15 |
| Pro | CCT | 72.00 | 3.42 | 0.08 |
| Pro | CCC | 626.00 | 29.71 | 0.68 |

Figure 9 A

Codon usage for enteric bacterial (highly expressed) genes
7/19/83

| AmAci d | Codon | Number | /1000 | Fraction . . |
|------------|-------|--------|-------|--------------|
| Gly | GGG | 13.00 | 1.89 | 0.02 |
| Gly | GGA | 3.00 | 0.44 | 0.00 |
| Gly | GGU | 365.00 | 52.99 | 0.59 |
| Gly | GGC | 238.00 | 34.55 | 0.38 |
| Glu | GAG | 108.00 | 15.68 | 0.22 |
| Glu | GAA | 394.00 | 57.20 | 0.78 |
| Asp | GAU | 149.00 | 21.63 | 0.33 |
| Asp | GAC | 298.00 | 43.26 | 0.67 |
| Val | GUG | 93.00 | 13.50 | 0.16 |
| Val | GUA | 146.00 | 21.20 | 0.26 |
| Val | GUU | 289.00 | 41.96 | 0.51 |
| Val | GUC | 38.00 | 5.52 | 0.07 |
| Ala | GCG | 161.00 | 23.37 | 0.26 |
| Ala | GCA | 173.00 | 25.12 | 0.28 |
| Ala | GCU | 212.00 | 30.78 | 0.35 |
| Ala | GCC | 62.00 | 9.00 | 0.10 |
| Arg | AGG | 1.00 | 0.15 | 0.00 |
| Arg | AGA | 0.00 | 0.00 | 0.00 |
| Ser | AGU | 9.00 | 1.31 | 0.03 |
| Ser | AGC | 71.00 | 10.31 | 0.20 |
| Lys | AAG | 111.00 | 16.11 | 0.26 |
| Lys | AAA | 320.00 | 46.46 | 0.74 |
| Asn | AAU | 19.00 | 2.76 | 0.06 |
| Asn | AAC | 274.00 | 39.78 | 0.94 |
| Met | AUG | 170.00 | 24.68 | 1.00 |
| Ile | AUA | 1.00 | 0.15 | 0.00 |
| Ile | AUU | 70.00 | 10.16 | 0.17 |
| Ile | AUC | 345.00 | 50.09 | 0.83 |
| Thr | ACG | 25.00 | 3.63 | 0.07 |
| Thr | ACA | 14.00 | 2.03 | 0.04 |
| Thr | ACU | 130.00 | 18.87 | 0.35 |
| Thr | ACC | 206.00 | 29.91 | 0.55 |
| Trp | UGG | 55.00 | 7.98 | 1.00 |
| End | UGA | 0.00 | 0.00 | 0.00 |

